REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining in this application be allowed.

Amendments

Claim 19 has been amended to direct the claim solely to methods for the treatment or prophylaxis of inflammatory conditions by up-regulating the *in vivo* generation of anti-inflammatory Th-2 derived cytokines and/or down regulating the *in vivo* generation of pro-inflammatory Th-1 derived cytokines thereby reducing the level of inflammation in the treated patient. Support for this amendment is found in originally presented Claim 1 as well as in Applicant's specification at, for instance, Examples 1 and 2 and, in particular, page 16, lines 3-16.

Newly added Claim 46 corresponds to now presented Claim 19 with the exception that this claim recites specific disease conditions from which the inflammation arises. Support for this amendment is found in Claim 19 as previously presented.

Newly added Claims 47-57 correspond to previously presented Claims 20-30.

No new matter has been added and, accordingly, entry of these amendments is requested.

Applicants note that the amendments to Claim 19 are entered solely to present what is believed to be allowable subject matter. Applicants reserve the right to file a continuation application directed to the previously presented subject matter.

Status of Claims

Claims 19-30 were previously in this application. Claim 19 has now been amended and Claims 46-57 have been added by this amendment. Accordingly, Claims 19-30 and 46-57 are

presented for further examination. A conformed copy of the pending claims is attached for the convenience of the Examiner.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 19, and its dependent claims, stand rejected under 35 U.S.C. §112, second paragraph, for the recitation of "the patient," in line 5 of claim 19, allegedly with insufficient antecedent basis. (Office Action of August 21, 2003 at page 4). Applicants submit that this rejection has been obviated by the amendments entered to Claim 19 wherein adequate antecedent basis for the term "patient" has been provided.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 19, and its dependent claims, stand rejected under 35 U.S.C. §112, first paragraph, as allegedly non-enabled for disease conditions other than contact hypersensitivity. For the following reasons, this rejection is traversed.

As noted above, the claims have been amended to recite methods for the treatment or prophylaxis of inflammatory conditions by up-regulating the *in vivo* generation of anti-inflammatory Th-2 derived cytokines and/or down-regulating the *in vivo* generation of pro-inflammatory Th-1 derived cytokines thereby reducing the level of inflammation in the treated patient. Claim 46 further recites specific disease conditions treated by the claimed methods.

Applicants submit that the now presented claims are enabled because they are limited to inflammatory conditions treated by up-regulating the *in vivo* generation of anti-inflammatory Th-2 derived cytokines and/or down regulating pro-inflammatory Th-1 derived cytokines. The data of Examples 1 and 2 clearly demonstrate that the claimed methods effect reduction in inflammation using an art recognized test for inflammation mediated by a Th-1 pathway. Further, as is well known, the specification is directed to one skilled in the relevant art and the skilled artisan recognizes that inflammatory cytokines play a distinct role in disease conditions manifesting inflammation as one of its conditions as evidenced by the following:

Adorini, "Interleuken-12, a key cytokine in TH-1-mediated autoimmune diseases," *CMLS Cell. Mol. Life. Sci.* 55: 1610-1625 (1999).. This reference discloses the role of the pro-inflammatory cytokine IL-12 in general in association with autoimmune diseases;

Taylor, "Anti-TNF alpha therapy for rheumatoid arthritis: an update," *Internal Medicine* 42(1): 15-20 (2003). This reference discloses the role of the pro-inflammatory TNF alpha cytokine in the inflammatory component of rheumatoid arthritis.

DeFougerolles, et al., "Reduction of inflammation...in models of hypersensitivity and arthritis." *The Journal of Clinical Investigation* 106(6): 721-729 (2000). This reference discloses a connection between contact hypersensitivity and arthritis through inflammatory responses.

Perlman, et al., "IL-6...regulated by Kinase inhibitor P21," *The Journal of Immunology* 170: 838-845 (2003). This reference shows the involvement of the pro-inflammatory IL-6 cytokine in rheumatoid arthritis.

Spadaro, "The role of interleukin-12 in immune-mediated rheumatoid diseases," *Reumotismo* 54(2): 113-121 (2002). This reference shows the role of the pro-inflammatory IL-12 in rheumatic diseases.

Park, et al., "Shift toward TH-1 cytokines ... in rheumatoid arthritis," *Arthritis & Rhematism* 44(3): 569-569 (2001). This reference shows the role of IFN gamma, and pro-inflammatory cytokines IL-12 and IL-4 in rheumatoid arthritis.

Peeva, et al. "Rheumatoid arthritis exacerbation caused by exogenous IL-12," *Arthritis & Rheumatism* 42(2): 461-463 (2000). This reference shows the role of the pro-inflammatory cytokine IL-12 in rheumatoid arthritis.

In view of the above and other art,[1] Applicants maintain that the expression of pro-inflammatory cytokines is art recognized to be associated with a variety of inflammatory conditions including inflammation arising from arthritis, contact hypersensitivity, autoimmune diseases and the like. As a corollary to the above, down-regulation of the expression of pro-inflammatory cytokines would logically provide a beneficial role in the reduction of inflammation arising from such diseases as would the up-regulation of anti-inflammatory cytokines. Accordingly, the data in Examples 1 and 2 of the specification enables for the now claimed invention as this data correlates reduction in inflammation using apoptotic bodies with

[1] If deemed necessary by the Office, Applicants are prepared to provide a more exhaustive list of references correlating inflammation in a variety of diseases with the expression of pro-inflammatory cytokines.

the up-regulation of the *in vivo* generation of anti-inflammatory Th-2 derived cytokines and/or down regulation of the *in vivo* generation of pro-inflammatory Th-1 derived cytokines.

The Office Action alleges that the diseases recited in previously presented Claim 19 are non-enabled because "many of the diseases are notoriously difficult to treat" (page 3 of the Office Action). However, such an allegation misses the point. Applicant is not claiming a method for treating contact hypersensitivity, psoriasis, rheumatoid arthritis, scleroderma, lupus, diabetes mellitus, organ rejection, miscarriage, multiple sclerosis, inflammatory bowel disease, and graft versus host disease in any therapeutic sense, i.e., recovery of the patient from these diseases. Rather, the claimed invention is directed to treating the inflammation arising from such diseases which is akin to treating the symptoms and not the underlying disease modality. The specification clearly supports that the administration of apoptotic bodies to the patient reduces inflammation arising from an art accepted model for a Th-1 inflammatory disorder (specification at page 13, lines 4-15).

Further, and more to the point, the Office Action fails to present any basis or reasoning as to why inflammation is not treated or reduced by modulating the expression of anti-inflammatory Th-2 derived cytokines and/or pro-inflammatory Th-1 derived cytokines. Such evidence of reasoning is a prerequisite to sustain a rejection under 35 U.S.C. §112, second paragraph. See, e.g., MPEP 216.04.

In view of the above, withdrawal of this rejection is requested.

Applicants submit that this application is now in condition for allowance. A notice to that effect is earnestly solicited.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant(s) petition(s) for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-2859** referencing docket no. 559082001800.

Respectfully submitted,

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CONFORMED COPY OF THE PENDING CLAIMS

19. A method for treatment and/or prophylaxis of inflammation in a mammalian patient which method comprises administering to said patient an effective amount of apoptotic bodies to up-regulate the *in vivo* generation of anti-inflammatory Th-2 derived cytokines and/or down regulate the *in vivo* generation of pro-inflammatory Th-1 derived cytokines thereby reducing the level of inflammation in the treated patient.

20. The method of claim 19, wherein the apoptotic bodies are in a liquid suspension along with viable cells.

21. The method of claim 20, wherein the apoptotic bodies comprise from 10% to 90% of the cellular portion of the suspension.

22. The method of claim 21, wherein the apoptotic bodies comprise from 30% to 70% of the cellular portion of the suspension.

23. The method of claim 19, wherein the apoptotic bodies are derived from extracorporeal treatment of blood cells compatible with those of the mammalian patient.

24. The method of claim 19, wherein the apoptotic bodies are derived from established cultured cell lines.

25. The method of claim 23, wherein the blood cells are white blood cells of blood compatible with that of the mammalian patient.

26. The method of claim 25, wherein the blood cells are the patient's own white blood cells.

27. The method of claim 26, wherein the blood cells are the patient's own T lymphocytes.

28. The method of claim 19, further comprising administering to a human patient a dosage of apoptotic bodies comprising from 10,000 to 10,000,000 apoptotic bodies per kilogram body weight of the patient.

29. The method of claim 28, wherein the dosage contains from 500,000 to 5,000,000 apoptotic bodies per kilogram body weight of the patient.

30. The method of claim 28, wherein the dosage contains from 1,500,000 to 4,000,000 apoptotic bodies per kilogram body weight of the patient.

46. A method for treatment and/or prophylaxis of inflammation in a mammalian patient with an inflammatory disorder, wherein the disorder is selected from the group consisting of contact hypersensitivity, psoriasis, rheumatoid arthritis, scleroderma, lupus, diabetes mellitus, organ rejection, miscarriage, multiple sclerosis, inflammatory bowel disease, and graft versus host disease, which method comprises administering to said mammalian patient an effective amount of apoptotic bodies to up-regulate the *in vivo* generation of anti-inflammatory Th-2 derived cytokines and/or down regulate the *in vivo* generation of pro-inflammatory Th-1 derived cytokines thereby reducing the level of inflammation in the treated patient.

47. The method of claim 46, wherein the apoptotic bodies are in a liquid suspension along with viable cells.

48. The method of claim 47, wherein the apoptotic bodies comprise from 10% to 90% of the cellular portion of the suspension.

49. The method of claim 48, wherein the apoptotic bodies comprise from 30% to 70% of the cellular portion of the suspension.

50. The method of claim 46, wherein the apoptotic bodies are derived from extracorporeal treatment of blood cells compatible with those of the mammalian patient.

51. The method of claim 46, wherein the apoptotic bodies are derived from established cultured cell lines.

52. The method of claim 50, wherein the blood cells are white blood cells of blood compatible with that of the mammalian patient.

53. The method of claim 52, wherein the blood cells are the patient's own white blood cells.

54. The method of claim 53, wherein the blood cells are the patient's own T lymphocytes.

55. The method of claim 46, further comprising administering to a human patient a dosage of apoptotic bodies comprising from 10,000 to 10,000,000 apoptotic bodies per kilogram body weight of the patient.

56. The method of claim 55, wherein the dosage contains from 500,000 to 5,000,000 apoptotic bodies per kilogram body weight of the patient.

57. The method of claim 55, wherein the dosage contains from 1,500,000 to 4,000,000 apoptotic bodies per kilogram body weight of the patient.